REMARKS

Corrections related to the Sequence Listing

Amendment to the specification is requested to insert the Sequence listing identifiers where appropriate.

Applicants have corrected the Sequence Listing as requested by the Examiner and enclose herewith a paper copy and CRF of the corrected Listing. The undersigned Applicants' representative hereby states that that the information recorded in Computer Readable Form (CFR diskette) is identical to the written (on paper) Sequence Listing and that they contain no new matter as required by 37 CFR 1.821(e)(f)(g) and 1.825(b)(d). The General Information portion of the sequence listing has been updated so as to contain information pertaining to the present application and to the priority application being claimed.

Response to Restriction Requirement

The Examiner has asserted that Weinacker *et al* teaches a fragment of β6 integrin subunit lacking the transmembrane and cytoplasmic domains wherein the fragment comprises a sequence capable of binding with a MAP kinase. The Examiner then argues that the different independent claims of the present application are not characterised by a single inventive concept, and has

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separated the claims into a significant number of groups which he considers constitute separate distinct inventions.

In order to expedite the progress of this application, please cancel claims 124 to 138, 140, 142, 155-162, 164-168, 170, 172-175, 178-184, 202-216, 226-235 and 239 without prejudice. Please also amend claim 139 to incorporate the limitations of claim 140 and amend the additional claims as set out herein. Support for the amendments, e.g., to claims 141, 143, 154, 220 and 221 is found in the specification at, for instance, page 54, line 16 to page 55, line 7, and no new matter has been added.

The Applicants traverse the restriction requirement in relation to the uncancelled claims. As stated at page 12, lines 2 to 7 of the specification, the present invention is based on the surprising finding that members of the mitogen activated protein (MAP) kinase family may associate with the cytoplasmic domain of integrin molecules. Integrins are transmembrane proteins expressed on the outer plasma membrane of cells. The present application describes the first indication that MAP kinases can bind to plasma membrane bound molecules. Prior to this, it was believed that MAP kinases only bound molecules remote from the plasma membrane which are downstream of receptor-initiated signalling events at the plasma membrane. MAP kinases modulate the function of many regulatory proteins including other protein kinases as well as transcription factors as stated in the

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specification at page 8, lines 16 to 21. As such, the action of MAP kinases is central to cellular function and inhibiting of the activity of MAP kinases can modulate the activity of a cell, including growth and proliferation. Recognition of the interaction between a MAP kinase and an integrin subunit such as β6 allows the rational design of agents which inhibit this interaction and thereby effect cellular activity (e.g., down regulation of cellular growth and proliferation). For example, a peptide consisting of the binding domain of the integrin for the MAP kinase can be used to block the binding of the MAP kinase and the integrin. The present invention, therefore, is not limited to the treatment of any particular disease or condition and has broad application.

The Weinacker citation merely teaches the provision of a truncated form of β6 lacking the transmembrane and cytoplasmic domains of the integrin subunit for the purpose of determining whether the cytoplasmic and transmembrane domains are necessary for binding to fibronectin. The article provides no teaching or suggestion whatsoever that a MAP kinase may bind with an integrin subunit such as β6 nor does the article disclose the binding domain for a MAP kinase in the cytoplasmic tail of β6 or of any other integrin subunit. In fact, Weinacker discards the cytoplasmic domain of β6. While the cytoplasmic domain of this

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integrin subunit incorporates a binding domain of, for instance, the MAP kinase Erk2, the binding domain comprises only a small segment of the overall cytoplasmic domain.

The remaining independent claims all relate to the binding interaction of a MAP kinase with a *binding domain* in the cytoplasmic domain of an integrin subunit. Applicants submit the claims as amended do not read on the Weinacker citation nor would a person skilled in the art be led to provide the subject matter now claimed in light of the disclosures provided by Weinacker. Accordingly, the remaining independent claims must be considered to be characterised by a single inventive concept.

If the Examiner finds that the Restriction Requirement still stands, Applicants elect the claims of Group XXIII, as amended, for prosecution at this time. These claims are all directed to a method for modulating activity of the cell comprising treating the cell with an effective amount of an agent that inhibits binding of a MAP kinase to a binding domain of an integrin for the MAP kinase. The dependent claims are all directed to preferred aspects of this inventive concept. Applicants also add herein new dependent claims 240 to 246 as indicated. Support for the new claims is found throughout the specification and in particular at page 12, lines 12 to 16; page 24, lines 7 to 9; page 24, line 19 to page 25, line 2; page 19, lines 11 to 16; page 49, line 16 to page 50, line 2; page 92, lines 1 to 13; and

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page 25, lines 4 to 9. No new matter has been added.

Applicants submit that all claims in the application are in condition for allowance and such action is requested.

The Examiner is encouraged to telephone the undersigned Applicant's representative to discuss any matter that would expedite the allowance of this case.

Respectfully submitted,

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